Where you deliver water and how is a powerful tool.
Philip Schmuck
quoted in *Conservation Foundation Letter,* May 1979

Forum

Yeast Gene and Cadmium

For almost 20 years, the field of phytoremediation has explored ways to use plants to extract toxic materials from soil. Recent advances may offer the promise of economical alternatives to the traditional, labor-intensive phytoremediation technique of removing and incinerating contaminated earth. Most researchers in the field are focused on identifying and refining naturally occurring plants that concentrate pollutants, typically heavy metals, in their cells. But recent work with fission yeast may lead to another potential route—albeit a long one—through which genetic engineering would result in new strains of high-yield, metal-accumulating plants. This work also may be useful for identifying plants that can better tolerate and store metals, says David Ow, a molecular geneticist at the Plant Gene Expression Center of the U.S. Department of Agriculture's Agricultural Research Service in Berkeley, California, and the University of California at Berkeley.

Ow's group has identified the mechanism and the gene responsible for the capability of a fission yeast, *Schizosaccharomyces pombe*, to move the heavy metal cadmium across its cell membranes. For some time, scientists have known that *S. pombe* behaves much like certain plants and fungi that have developed coping strategies for surviving in metal-rich environments fatal to most organisms. *S. pombe* responds to cadmium by producing small peptides called phytochelatins that are rich in the amino acid cysteine. These phytochelatins bond with the cadmium ions, which allows them to transport the ions across cell membranes and into the yeast's vacuole, where the metal accumulates. Once in the vacuole, the ion-peptide complex stabilizes as a crystallite. This "cellular trashbag" can swell with metals until cadmium accounts for as much as 90% of the cell's volume, Ow says.

To isolate the gene responsible for this behavior, Ow compared normal *S. pombe* to cadmium-sensitive *S. pombe* mutants. The mutant yeast failed to chelate, it turned out, because they lack a single gene—dubbed *HMT1*, for "heavy metal tolerance"—which codes for the critical peptide. Now that Ow knows how *S. pombe* triggers the production of the phytochelatins, he is investigating exploiting this cellular "pump" through two angles. One way may be to bioengineer the yeast gene into plants that already tolerate heavy metals well enough to survive in polluted soil, but that aren't so-called "hyperaccumulators" of metals. Another way may be to identify an equivalent gene already present in metal-tolerant plants.

"The neat thing about it in yeast is that if you overproduce this [peptide], you get an increased rate of transport," Ow explains. "[The yeast] also ends up accumulating more metals in the vacuole, while at the same time becoming more resistant to cadmium. So the hunt is now on to look for a similar protein in plants. Assuming that the whole system is analogous, there should be a similar protein. If we can clone it out and overproduce it so that the plant makes lots more of these proteins, we may be able to pump more metals into the vacuole. Therefore, the plant can pick up more metals as a whole."

Genetically engineering such plants is important, Ow says, because although unaltered hyperaccumulators concentrate heavy metals at high levels (up to 1% of dry weight for cadmium and 5% for zinc and nickel), the plants themselves are too small to extract significant quantities of pollutants.

Other researchers, however, aren't so sure. "I can do more phytoremediation with natural metal-hyperaccumulator plants than they have any hope of doing with these plants that don't have the genetic capability," says research agronomist Rufus Chaney of the U.S. Department of Agriculture's environmental chemistry lab in Beltsville, Maryland. Engineering plants to collect more metals is not useful if those metals collect in the roots, which cannot be harvested practically, Chaney says. Furthermore, he continues, it's not necessarily a simple matter to switch the metal collection site from the plant's roots to its shoots. Finally, he says, "Obtaining expression of this gene at high levels in the membrane of xylem parenchyma cells to pump metals from the cytoplasm into the xylem would [require] further novel bioengineering . . . to make this gene relevant to phytoremediation rather than [merely] trapping cadmium in the roots."

According to Ilya Raskin, a Rutgers University molecular biologist, current phytoremediation techniques don't depend heavily on the process Ow has identified. Instead, workers treat contaminated soil to dissolve metals and produce a soil solution that metal-resistant plants can draw in through their roots, concentrating metals that are then harvested. Says Raskin, "It's a collection system and it doesn't rely on intricate cellular processes of metal transport." Still, he says, "Only history will tell whether [the cadmium research] will . . . have any relevance to phytoremediation.

Changes to Classifying Carcinogens

Everyone knows that saccharin causes cancer, right? Wrong, according to the National Toxicology Program (NTP), which is expected to delist the chemical from the ninth *Report on Carcinogens*, where it has been classified as "Reasonably Anticipated to Be a Human Carcinogen" since 1981. In the same review, to be held 30–31 October 1997 at the NIEHS, the NTP Board of Scientific Counselors' *Report on Carcinogens* Subcommittee will also examine the toxicity data on 13 other substances, and will expand the traditional scope of substances eligible for consideration for listing in the *Report on Carcinogens* to include chemical mixtures (such as in smokeless tobacco products) and exposure circumstances (such as UV radiation).

The NTP is required by law to prepare a report that contains a list of all substances that are either known to be human carcinogens or may reasonably be anticipated to be human carcinogens and to which a significant number of persons residing in the United States are exposed. The law also states that these reports should provide available information on the nature of exposure, the estimated number of persons exposed, and the extent to which the implementation of federal regulations decreases the risk to public health from exposures to these chemicals. The eighth volume of this report is nearing completion and is scheduled to be published later this year.

The preparation of the ninth report differs from previous reports in several significant ways. Traditionally, the *Report on Carcinogens*, unlike the *Monographs on the Evaluation of Carcinogenic Risks to Humans* prepared by the International Agency for Research on Cancer (IARC), have not examined and discussed evidence for the carcinogenicity of manufacturing processes and